Influence of comorbid alcohol use disorders on the clinical patterns of major depressive disorder: A general population-based study

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ABSTRACT

Background: To compare the symptom patterns of major depressive disorder (MDD) among subjects with MDD and 1) no alcohol use disorder (AUD), 2) alcohol abuse and 3) alcohol dependence, respectively.

Methods: In a general population survey of 38,694 French individuals, MDD and AUDs were assessed using the Mini International Neuropsychiatric Interview 5.0.0 (MINI). A total of 4339 subjects (11.2%) in the sample met the criteria for MDD. Among them, 413 (9.5%) AUD subjects were identified: 138 (3.2%) for alcohol abuse and 275 (6.3%) for alcohol dependence. The associations of each of the ten MDD criteria of the MINI and psychiatric clinical features were compared among the three groups. The relative profiles of ‘MDD + AUD’ vs. ‘MDD alone’ were determined using a multivariable stepwise regression model.

Results: With the noAUD group as the reference, sadness (OR = 0.46; 95%CI, 0.29–0.74) and anhedonia (OR = 1.66; 95%CI, 1.06–2.73) were only associated with alcohol abuse. Sleep disorders (OR = 2.07; 95%CI, 1.51–2.88), feelings of guilt (OR = 1.41; 95%CI, 1.05–1.90), diminished concentration/indecisiveness (OR = 1.52; 95%CI, 1.12–2.07) and thoughts of death (OR = 1.95; 95%CI 1.49–2.55) were only associated with alcohol dependence. Weight or appetite variations were both associated with alcohol abuse (OR = 1.7; 95%CI, 1.15–2.53) and dependence (OR = 1.41; 95%CI, 1.06–1.88). Bipolar disorder and PTSD were only associated with alcohol dependence. Psychotic features, previous suicide attempts, and panic disorder were more frequent in the MDD-AUD group.

Conclusion: MDD-AUD subjects displayed a more severe profile with specific symptomatology and comorbidity profiles compared to MDD-only subjects.
1. Introduction

Dual diagnoses are specific clinical entities that do not merely consist of the simple adding of characteristics of each underlying disorder but also possess specific vulnerability factors, specific outcomes, and specific clinical features (Brady et al., 2007; Morojele et al., 2012). The association between major depressive disorder (MDD) and alcohol use disorders (AUDs), i.e., alcohol dependence or abuse, is one of the most common types of dual diagnoses. Bidirectional chronological relationships have been found in the co-occurrence of MDD and AUDs (Gilman and Abraham, 2001; Pacek et al., 2013). A stronger association has been reported between alcohol dependence and MDD compared to the association between alcohol abuse and MDD (Cranford et al., 2011; Dawson et al., 2005; Grant and Harford, 1995; Pacek et al., 2013). Compared to MDD and AUDs alone, comorbid AUDs and MDD also display specifically worse outcomes, including a shorter time to rehospitalization (Lin et al., 2007), an elevated risk of premature death due to suicide or other unnatural death (Yoon et al., 2011), or lower global functioning and dissatisfaction (Brière et al., 2014).

Moreover, the MDD criteria encompass a group of disorders that are heterogeneous with respect to their supposed pathophysiology and clinical expression (Hasler et al., 2004). Indeed, different forms of MDD have been associated with distinct biological, psychological, and behavioral correlates and potentially distinct etiologies (Fontoulakis et al., 2004; Gottesman and Gould, 2003; Leventhal et al., 2008). It is therefore important to analyze the specificities of the clinical profile of MDD associated with AUDs compared to MDD without AUDs based on individual key MDD symptoms. This would allow the isolation of phenotype markers, possibly representing more direct expressions of underlying genes, neurophysiology, and psychosocial processes, thus identifying endophenotypes of this heterogeneous MDD entity (Gottesman and Gould, 2003; Hasler et al., 2004; Leventhal et al., 2011).

To our knowledge, few previous studies have focused on the difference in the distribution of the diagnostic criteria for MDD between expressions with and without AUDs or even SUDs (Blanco et al., 2012; Cornelius et al., 1995; Davis et al., 2006). In those studies, individuals with MDD and SUDs presented with a larger number of DSM-IV MDD criteria than those with MDD alone. Moreover, they displayed more symptoms, such as sleep disorders, feelings of worthlessness, loss of interest, thoughts of death, and suicide attempts, but were less likely to report sadness (Blanco et al., 2012). According to the ICD-30 criteria (30-item Inventory of Depressive Symptomatology-Clinician Rated), MDD-SUDs subjects presented more irritable moods, mood variation, negative outlook of oneself, sympathetic arousal and gastrointestinal symptoms (Davis et al., 2006). Furthermore, depressive symptoms, such as suicidality and low self-esteem, were more pronounced among MDD subjects with alcohol dependence (Cornelius et al., 1995). Overall, previous studies did not distinguish between alcohol dependence and abuse. Moreover, they were not based on multivariable modeling, especially for controlling other clinical dimensions of MDD (e.g., previous suicide attempts or bipolar or psychotic characteristics) or other comorbid associations (e.g., other SUDs or comorbid anxiety disorder).

In the present study, we explored the distribution of the clinical criteria for MDD among MDD subjects with and without AUDs using a French general population survey. We also explored other clinical features of MDD and other comorbidities, and we built a step-by-step multivariable model that explored the global clinical profile of the MDD-AUD association. The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Von Elm et al., 2007) (see Supplemental material STROBE statement).

We hypothesized that MDD-AUDs will present a more severe profile than MDD without AUDs with a gradient of severity where the MDD-alcohol abuse group experiences greater severity than MDD without AUD and less severity than the MDD-alcohol dependence group.
were conducted, with each of the categorical clinical features of MDD being the dependent variable and the predefined groups being the independent variable. Sociodemographic variables that were found to be associated with a significance level of $\alpha = 0.2$ with at least one MDD symptom in the bivariate analyses were included in all binomial logistic regressions as adjustment variables. Because a comorbid SUD might substantially alter the result analyses, comorbid SUDs were included as an a priori adjustment factor, and sensitivity analyses were conducted using the sample without subjects with a comorbid SUD. Moreover, because bipolar disorder has a specific profile regarding both the clinical criteria of depression and the addictive and anxiety comorbidities (Baethge et al., 2005; Furukawa et al., 2000; Geoffroy et al., 2017), sensitivity analyses were conducted using the sample without subjects with bipolar disorder. For all these analyses, we also indicate of the variables that met statistical significance after applying a Bonferroni correction for multiple testing.

Furthermore, a multivariable backward step-by-step regression model was built, with the AUD group variable being the dependent variable. The independent variables initially included in the model consisted of 1) the ten MDD clinical features, 2) the different sociodemographic variables, 3) bipolar disorder, 4) psychotic characteristics, 5) comorbid SUD and 6) each of the different anxiety disorders. At each step, the least significant variable was removed to compute the next step. The best fitting model with all significant independent variables (at a level of $\alpha = 0.05$) was retained.

All statistical analyses were performed using R software (http://www.R-project.org/).

3. Results

3.1 Descriptive statistics

The detailed sociodemographic characteristics of the MDD sample can be found in Table 1.

In total, 208 MDD subjects (4.8%) met the criteria for bipolar disorder, while 1578 subjects (36.4%) reported lifetime psychotic symptoms, and 756 individuals (17.4%) reported previous suicide attempts. Finally, 864 subjects (19.9%) met the criteria for panic disorder, while 522 subjects (12.0%) met the criteria for social phobia, 1278 subjects (29.5%), for GAD, and 92 subjects, (2.1%), for PTSD.

3.2 Results of the analyses on MDD diagnostic criteria

All sociodemographic variables were significantly associated with at least one of the ten clinical criteria for MDD, and they were thus all included in the multivariable logistical binomial regression analyses. The results of the analyses comparing the frequency of the ten clinical criteria for MDD according to the AUD status can be found in Table 2 (sample includes subjects with comorbid SUDs) and Table 3 (sample excludes subjects with comorbid SUDs). Each of the categorical clinical features of MDD was the dependent variable and the predefined groups being the independent variables. Analyses were adjusted on marital status, level of income, level of education and native variable.

In the sample that included subjects with comorbid SUDs (Table 2) and with the group ‘noAUD’ as the reference, sadness was negatively associated with alcohol abuse (OR = 0.46; 95%CI, 0.29–0.74) but not with alcohol dependence. Anhedonia was positively associated with alcohol abuse only (OR = 1.66; 95%CI, 1.06–2.73), while weight or appetite variations were positively associated with alcohol abuse (OR = 1.70; 95%CI, 1.15–2.53) and alcohol dependence (OR = 1.41; 95%CI, 1.06–1.88, respectively). Furthermore, several clinical features of MDD were positively associated only with alcohol dependence: sleep disorders (OR = 2.07; 95%CI, 1.51–2.88), feelings of guilt (OR = 1.41; 95%CI, 1.05–1.99), diminished concentration/indecisiveness (OR = 1.52; 95%CI, 1.12–2.07) and thoughts of death (OR = 1.95; 95%CI, 1.49–2.55). After the Bonferroni correction, all associations remained significant, except the associations between anhedonia and alcohol abuse, between weight or appetite variations and both AUDs, and between feelings of guilt, diminished concentration/indecisiveness and alcohol dependence.

In the sample that excluded subjects with comorbid SUDs (Table 3), anhedonia was no longer associated with alcohol abuse, and weight and appetite variations were no longer associated with alcohol dependence. Conversely, feelings of worthlessness were positively associated with

Table 1
Sociodemographic characteristics of subjects with and without AUDs

<table>
<thead>
<tr>
<th></th>
<th>MDD without AUDs (N = 3926)</th>
<th>MDD with AUDs (N = 413)</th>
<th>MDD with alcohol abuse (N = 138)</th>
<th>MDD with alcohol dependence (N = 275)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (standard deviation)</td>
<td>43.9 (18.9)</td>
<td>36.7 (13.2)</td>
<td>36.8 (13.1)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Gender (%)</td>
<td>Male</td>
<td>33.9</td>
<td>71.0</td>
<td>72.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>66.1</td>
<td>29.0</td>
<td>27.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Education level (%)</td>
<td>No education-elementary level</td>
<td>27.8</td>
<td>20.3</td>
<td>21.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>College level</td>
<td>52.3</td>
<td>64.5</td>
<td>61.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>University level</td>
<td>19.8</td>
<td>15.2</td>
<td>17.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Income level (%)</td>
<td>Low</td>
<td>52.3</td>
<td>56.7</td>
<td>62.1</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>34.1</td>
<td>29.9</td>
<td>29.6</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>13.6</td>
<td>13.4</td>
<td>8.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Marital status (%)</td>
<td>Married</td>
<td>43.7</td>
<td>32.1</td>
<td>26.1</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Never married</td>
<td>32.1</td>
<td>46.7</td>
<td>47.8</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Separated</td>
<td>12.0</td>
<td>19.0</td>
<td>21.7</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Widowed</td>
<td>12.2</td>
<td>2.2</td>
<td>4.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Native variable</td>
<td>French/Native</td>
<td>92.9</td>
<td>97.8</td>
<td>91.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>1GM</td>
<td>7.1</td>
<td>2.2</td>
<td>8.4</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* MDD: Major Depressive Disorder.  
** AUDs: Alcohol Use Disorders.  
# Native: born in metropolitan France.  
$1GM$: First-generation migrant, i.e. born outside metropolitan France.  
$*$ Comparisons between MDD with AUD and without AUD using the t-test and chi-squared test.
Sensitivity analyses: Comparison of rates of MDD symptoms, clinical features and anxiety comorbidities according to the AUD status

<table>
<thead>
<tr>
<th>MDD symptoms</th>
<th>noAUD Group</th>
<th>Alcohol Abuse Group</th>
<th>Alcohol Dependence Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% OR [95% CI]</td>
<td>% OR [95% CI]</td>
<td>% OR [95% CI]</td>
</tr>
<tr>
<td>Sadness</td>
<td>91.0</td>
<td>81.2 0.46 [0.29-0.74] *</td>
<td>89.1 0.93 [0.61-1.46]</td>
</tr>
<tr>
<td>Anhedonia</td>
<td>75.2</td>
<td>82.6 1.66 [1.06-2.73] **</td>
<td>80.7 1.27 [0.92-1.78]</td>
</tr>
<tr>
<td>Fatigue or loss of energy</td>
<td>86.7</td>
<td>87.0 1.16 [0.71-2.00] **</td>
<td>83.6 0.96 [0.67-1.40]</td>
</tr>
<tr>
<td>Weight or appetite variations</td>
<td>59.4</td>
<td>72.5 1.70 [1.15-2.53] **</td>
<td>68.7 1.41 [1.06-1.88]</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>67.2</td>
<td>69.6 1.18 [0.81-1.75] **</td>
<td>78.5 2.07 [1.51-2.88] **</td>
</tr>
<tr>
<td>Psychomotor retardation or agitation</td>
<td>53.8</td>
<td>55.8 1.09 [0.77-1.56] **</td>
<td>61.1 1.29 [0.99-1.70]</td>
</tr>
<tr>
<td>Feelings of worthlessness</td>
<td>61.9</td>
<td>60.1 0.88 [0.62-1.27] **</td>
<td>66.7 1.20 [0.91-1.60]</td>
</tr>
<tr>
<td>Feelings of guilt</td>
<td>59.4</td>
<td>68.1 1.23 [0.85-1.82] **</td>
<td>73.0 1.41 [1.05-1.90]</td>
</tr>
<tr>
<td>Diminished concentration/indecisiveness</td>
<td>66.0</td>
<td>67.4 1.01 [0.70-1.49] **</td>
<td>76.4 1.52 [1.12-2.07]</td>
</tr>
<tr>
<td>Thoughts of death</td>
<td>37.6</td>
<td>42.0 1.19 [0.83-1.71] **</td>
<td>53.8 1.95 [1.49-2.55] **</td>
</tr>
</tbody>
</table>

**p-value < 0.005. * p-value < 0.05. ** p-value < 0.0005. + Significant after Bonferroni correction (i.e. at a level α = 0.0029).

Table 3

Sensitivity analyses: Comparison of rates of MDD symptoms, clinical features and anxiety comorbidities according to AUD status in the sample without SUDs

<table>
<thead>
<tr>
<th>MDD symptoms</th>
<th>NoAUD Group</th>
<th>Alcohol Abuse Group</th>
<th>Alcohol Dependence Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% OR [95% CI]</td>
<td>% OR [95% CI]</td>
<td>% OR [95% CI]</td>
</tr>
<tr>
<td>Sadness</td>
<td>91.0</td>
<td>81.0 0.43 [0.27-0.72] **</td>
<td>87.3 0.77 [0.49-1.26]</td>
</tr>
<tr>
<td>Anhedonia</td>
<td>75.2</td>
<td>80.1 1.46 [0.91-2.44] **</td>
<td>81.2 1.30 [0.90-1.94]</td>
</tr>
<tr>
<td>Fatigue or loss of energy</td>
<td>86.7</td>
<td>87.0 1.20 [0.70-1.28] **</td>
<td>84.6 1.10 [0.73-1.73]</td>
</tr>
<tr>
<td>Weight or appetite variations</td>
<td>59.2</td>
<td>72.4 1.67 [1.11-2.58] **</td>
<td>66.5 1.53 [0.97-1.85]</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>67.5</td>
<td>72.4 1.34 [0.88-2.08] **</td>
<td>77.6 1.87 [1.31-2.74] **</td>
</tr>
<tr>
<td>Psychomotor retardation or agitation</td>
<td>53.7</td>
<td>56.0 1.12 [0.76-1.65] **</td>
<td>57.9 1.17 [0.86-1.59]</td>
</tr>
<tr>
<td>Feelings of worthlessness</td>
<td>65.8</td>
<td>67.2 1.06 [0.71-1.61] **</td>
<td>74.1 1.40 [1.01-1.99]</td>
</tr>
<tr>
<td>Feelings of guilt</td>
<td>58.8</td>
<td>65.5 1.19 [0.80-1.61] **</td>
<td>71.4 1.44 [1.04-2.01]</td>
</tr>
<tr>
<td>Diminished concentration/indecisiveness</td>
<td>65.8</td>
<td>67.2 1.06 [0.71-1.61] **</td>
<td>74.1 1.40 [1.01-1.99]</td>
</tr>
<tr>
<td>Thoughts of death</td>
<td>37.7</td>
<td>39.7 1.10 [0.74-1.63] **</td>
<td>52.8 1.92 [1.42-2.62] **</td>
</tr>
</tbody>
</table>

**p-value < 0.005. * p-value < 0.05. ** p-value < 0.0005. + Significant after Bonferroni correction (i.e. at a level α = 0.0029).

Abbreviations: MDD: Major Depressive Disorder; AUDs: Alcohol Use Disorders; GAD: Generalized anxiety disorder; PTSD: Posttraumatic stress disorder; OR: Odds-Ratio; CI 95%: 95% confidence interval.

OR and 95% CI result from multivariable logistical binomial regression with each of the categorical clinical features of MDD being the dependent variables and alcohol abuse and dependence being the independent variables. AUD status reference category was no AUD. Analyses were adjusted on marital status, level of income, level of education and native variable.

Abbreviations: MDD: Major depressive disorder; AUDs: Alcohol use disorders; OR: Odds-ratio; GAD: Generalized anxiety disorder; PTSD: Posttraumatic stress disorder; SUDs: Substance Use Disorders; OR: Odds-ratio; CI 95%: 95% confidence interval.

OR and 95% CI result from multivariable logistical binomial regression with each of the categorical clinical features of MDD being the dependent variables and alcohol abuse and dependence being the independent variables. AUD status reference category was no AUD. Analyses were adjusted on marital status, level of income, level of education and native variable.
alcohol dependence (OR = 1.40; 95%CI, 1.01–1.99). After the Bonferroni correction, all associations remained significant, except the associations between weight and appetite variations and alcohol abuse and between feelings of worthlessness, feelings of guilt, diminished concentration/indecisiveness and alcohol dependence.

In the sample that excluded bipolar disorder (Table 4), before the Bonferroni correction, all associations remained significant (in comparison to Table 2), except for weight and appetite variations, feeling of guilt and alcohol dependence. However, the association between feelings of worthlessness and alcohol dependence became significant (OR = 1.29, p < 0.001). After the Bonferroni correction, this sample, sadness was no longer associated with alcohol abuse.

3.3. Results of the analyses on other characteristics of the MDD population

Bipolar disorder was associated only with alcohol dependence (OR = 2.18; 95%CI, 1.42–3.30). Psychotic characteristics and previous suicide attempts were associated with both alcohol abuse (respectively, OR = 2.31 95% CI, 1.59–3.39 and OR = 2.24; 95%CI, 1.45–3.41) and alcohol dependence (OR = 1.90; 95%CI, 1.44–2.53 and OR = 2.94; 95%CI, 2.17–3.98) (Table 2). The results were similar in the sample without SUDs (Table 3). After the Bonferroni correction, all associations remained significant in the samples with and without SUD (Table 3).

Panic disorder was associated with alcohol abuse (OR = 1.63; 95%CI, 1.08–2.43) and alcohol dependence (OR = 1.91; 95%CI, 1.41–2.56). PTSD was associated only with alcohol dependence (OR = 3.19; 95%CI, 1.70–5.72) but not alcohol abuse (Table 2). The results were similar in the sample without SUDs (Table 3). After the Bonferroni correction, all associations remained significant, except for the association between panic disorder and alcohol abuse.

In the sample that excluded bipolar disorder (Table 4), before the Bonferroni correction, all associations remained significant (in comparison to Table 2). The association between PTSD, and alcohol abuse became significant (OR = 3.13 95%CI, 1.15–7.21). After the Bonferroni correction, all associations remained significant except for previous suicide attempts, panic disorders, PTSD, and alcohol abuse.

3.4. Results of the backward step-by-step regression modeling

In total, 24 variables (i.e., six sociodemographic variables, the SUD status, the ten MDD criteria, the three associated clinical features of MDD, and the three anxiety disorders variables) were included as explanatory variables in two stepwise descending analyses (one for alcohol abuse, one for alcohol dependence). This model progressively eliminates the explanatory variables not found statistically associated with the dependent variables. The last step of each analysis is presented in Table 5. Only the variables significantly associated with alcohol abuse or alcohol dependence are exhibited, and the reported associations are estimated taking into account all other variables included in the model.

4. Discussion

The main objective of the study was to compare the MDD symptom patterns and psychiatric comorbidities of subjects with a current MDD according to their AUD status using a cross-sectional survey of a French national community-based sample.

First, our overall data seem consistent with previous findings of the epidemiology of MDD, as we found a prevalence rate of 11.2% for MDD according to the MINI. If a previous study found a twelve-month MDD prevalence of 5.3% in the adult US population (Hasin et al., 2005), in the French population, however, the prevalence of last-month and twelve-month MDD has been found to be 5.3% in the adult US population (Hasin et al., 2005), in the French population, however, the prevalence of last-month and twelve-month MDD has been found to be 12% and 7.8%, respectively (Lamboy et al., 2007; Le Pape and Lecomte, 1999). The differences between French and US prevalence can be explained by the different methodologies and questionnaires used. Moreover, among US patients with MDD in the prior 12 months, 14% met the criteria for AUD, and nearly 5% met the criteria for SUDs (Hasin et al., 2005), which is
The AUD group variable is the dependent variable. The independent variables associated with alcohol abuse and dependence status. The results of the comparisons in the expression of the different symptom patterns of MDD according to the alcohol status, based on the NESARC sample without SUDs. By comparison, data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) found associations between 12-month AUDs and phobia based on the DSM-5 criteria did not find any association between PTSD and AUDs after controlling for socio-demographic features and other psychiatric disorders (Smith et al., 2016). Moreover, studies based on the NESARC found associations between 12-month AUDs and phobia but not with panic disorder, agoraphobia, GAD or PTSD. However, lifetime moderate and severe AUDs were associated with panic disorder and severe AUDs with PTSD, which is more consistent with our results (Grant et al., 2015). MDD subjects with AUDs may have a trauma history which makes them vulnerable to depression, or alternatively, may have a milder depression and a subsequent trauma event. Alcohol could have then been used to manage these chronic and comorbid symptoms (Bailey et al., 2012). The reasons for which panic disorder, but not GAD nor social phobia, was associated with alcohol dependence, remain unclear. It could reflect the fact that alcohol is used as self-medication for preventing panic attacks, and/or that alcohol dependence increases the likelihood of developing or maintaining panic disorder.

In our findings, experiencing bipolar disorder was specifically associated with alcohol dependence. This is consistent with a precedent study that found an association between AUDs and bipolar disorder among MDD subjects (Yoon et al., 2015). We also performed a sensitivity analysis that excluded the diagnosis of bipolar disorder, considering that MDD subjects with bipolar disorder could exhibit specific features of depression. After the Bonferroni correction, in the sample without bipolar disorder, sadness was no longer negatively associated with alcohol abuse, while previous suicide attempts were no longer positively associated with alcohol use.

Last, the results of the multivariable modeling of the clinical profile between MDD subjects without AUDs and alcohol abuse and dependence groups found that younger age and male gender were associated with both AUDs. These results are consistent with previous studies reporting an association between MDD-AUDs or MDD-SUDs and younger among MDD subjects with alcohol dependence, the level of alcohol use predicts the severity of insomnia (Zhabenko et al., 2013). Self-medication of insomnia with alcohol may be frequent among subjects with alcohol dependence, but there is a general scientific consensus that both acute and chronic alcohol use disrupt sleep patterns (Brower et al., 2001). However, the literature is relatively unclear on this point, and other previous studies did not find any difference in the occurrence of sleep disorders between MDD subjects with and without AUIDs or SUDs (Cornellius et al., 1995; Davis et al., 2006).

Furthermore, suicidal thoughts were another MDD symptom found specifically associated with alcohol dependence in our study. This is also consistent with previous studies reporting higher suicidal ideation and suicide attempts in MDD individuals with alcohol dependence (Cornellius et al., 1996, 1995; Sher et al., 2008, 2005). The mechanisms underlying this relationship are debated. A previous study hypothesized that the higher rate of ideal thoughts and suicide attempts in MDD subjects with alcohol dependence could be explain by a higher level of predisposing (aggression/impulsivity, severe alcoholism, negative affect and hopelessness) and precipitating factors (stressful life events, particularly interpersonal difficulties) (Conner and Duberstein, 2004; Sher et al., 2005).

In our study, other clinical features were compared in MDD subjects depending on the alcohol status. Associated psychotic characteristics were found to be more frequent in both the ‘alcohol abuse’ and ‘alcohol dependence’ groups compared to the ‘noAUD’ group. Sensitivity analyses did not provide substantially different results. Previous studies also found a strong association between AUDs and psychotic disorders, with over one-third of patients with schizophrenia presenting criteria for an AUD (Green and Brown, 2006; Regier et al., 1990). Concerning anxiety comorbidities, panic disorder and PTSD were associated only with alcohol dependence. No significant association was found between social phobia or GAD and AUDs. Overall, previous studies also found that in the general population, AUDs were significantly associated with anxiety disorder (Bailey et al., 2012; Fuehrlein et al., 2016; Suttajit et al., 2012). However, a recent study based on the DSM-5 criteria did not find any association between PTSD and AUDs after controlling for socio-demographic features and other psychiatric disorders (Smith et al., 2016). Moreover, studies based on the NESARC found associations between 12-month AUDs and phobia but not with panic disorder, agoraphobia, GAD or PTSD. However, lifetime moderate and severe AUDs were associated with panic disorder and severe AUDs with PTSD, which is more consistent with our results (Grant et al., 2015). MDD subjects with AUDs may have a trauma history which makes them vulnerable to depression, or alternatively, may have a milder depression and a subsequent trauma event. Alcohol could have then been used to manage these chronic and comorbid symptoms (Bailey et al., 2012). The reasons for which panic disorder, but not GAD nor social phobia, was associated with alcohol dependence, remain unclear. It could reflect the fact that alcohol is used as self-medication for preventing panic attacks, and/or that alcohol dependence increases the likelihood of developing or maintaining panic disorder.

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age (Davis et al., 2006, 2005; Sher et al., 2008) or male gender (Davis et al., 2006, 2005; Rodgers et al., 2014; Schuch et al., 2014). As we discussed before, sadness was strongly negatively associated with alcohol abuse, whereas separated marital status, sleep disorders and SUDs were strongly positively associated with alcohol dependence.

Overall, these results have several implications. In line with a dual-diagnosis approach, we found that MDD-AUD subjects, especially those with alcohol dependence, exhibit a specific clinical profile and presented much more frequent additional comorbidities, suggesting that they constitute a specific subpopulation with increased severity markers among MDD subjects.

The study has several limitations that should be addressed. First, the data collected were relatively old because the MHGP study ended in 2003. However, this limitation allowed direct comparison with the American NESARC cohort, which was more or less conducted in the same period. Moreover, it is unlikely that the specific clinical patterns of MDD subjects with AUDs may have specifically changed since 2003. Another possible limitation of the study was that the sampling was non-probabilistic and was performed using a quota within regions. However, several methodological precautions were taken in the MHGP survey to mitigate this issue, including the adjustment of each site’s subsample based on local data from the 1999 French Census (Caria et al., 2010; Cohidon, 2007). Moreover, numerous similar large-sample studies exploring mental health issues, including the NESARC, have also been based on a quota-sampling strategy, which yields the same sociodemographic characteristics as those of the general population. Moreover, the study has an observational cross-sectional design that does not permit causal inferences (Bradford-Hill, 1965). In addition, our multivariable model only included the most frequent psychiatric comorbidities, i.e., bipolar disorder, anxiety disorders, and other SUDs. However, some other comorbidities, like personality disorders, were not included, which can affect our main findings. Another possible limitation is that some participants may have incorrectly responded to the MINI interview concerning AUDs, which is relatively common due to the social desirability bias (Davis et al., 2010). Finally, the sample was limited to subjects who met the criteria for a full MDD. Future studies could more specifically compare the prevalence and clinical characteristics of individuals according to dimensional outcomes and subclinical depression.

5. Conclusion

In a French general population sample, MDD subjects with AUDs showed a more severe clinical profile with a wider array of symptoms and more comorbidities compared to MDD subjects without AUDs. This is in line with the “dual diagnosis” approach, according to which comorbid psychiatric and addictive disorders constitute specific entities with specific clinical features and increased severity factors. Moreover, our findings were the first to differentiate between alcohol abuse and dependence, thereby showing that alcohol abuse also exhibited some distinctive features and an overall clinical profile closer to that of ‘noAUD’ MDD subjects compared to those with alcohol dependence.

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Contributors

Jean-Luc Roelandt, Pierre Thomas and Guillaume Vaiva designed the MGHP survey. Imane Benradia and Jean-Luc Roelandt undertook data collection. Louise Carton managed the literature searches. Louise Carton, Benjamin Rolland and Baptiste Pignon wrote the first draft. Baptiste Pignon, Benjamin Rolland and Pierre A. Geoffroy designed and undertook statistical analyses. All authors reviewed and approved the final manuscript.

Conflicts of interest

Mickaël Naassila received honoraria or financial compensation as symposium speaker from Lundbeck, Indivior and Merck-Serono with no link with the submitted work. Louise Carton received honoraria as symposium speaker for Lundbeck and Indivior with no link with the submitted work. Other authors declare they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.drugalcdep.2018.02.009.

References
